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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/355,793	09/21/1999	MARTIN BLASER	D5979	6942

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PORTNER, VIRGINIA ALLEN

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

File Copy

Office Action Summary	Application No. 09/355,793	Applicant(s) Blaser et al
	Examiner Portner	Art Unit 1645

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jan 21, 2003* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 5-13, and 15-18* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 5-13, and 15-18* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1,11 and 18 have been amended.

Claims 1,5-13;15-17 and 18 are pending.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

CONTINUED EXAMINATION UNDER 37 CFR 1.114 AFTER FINAL REJECTION

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 21, 2003 has been entered

Drawings

3. This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

a. Please see attached US-PTO 948 form.

Specification

4. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Rejections Withdrawn

5. Claims 1,6-8 rejected under 35 U.S.C. 102(a) as being anticipated by Dworkin et al (March 1996), in light of the amendment of claim 1 to require the surface expression of the heterologous protein.

6. Claims 1, 6-8 rejected under 35 U.S.C. 102(b) as being anticipated by Blaser (November 1994), in light of the amendment of claim 1 to require the surface expression of the heterologous protein.

7. Claim 11 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, in light of the amendment of claim 11 to recite the phrase "DNA cassette inserted into the coding sequence of a sapA homolog of said strain and expression of said DNA cassette results in surface expression of a chimeric protein comprises said heterologous protein."

Rejections Maintained

8. Claims 1, 5-13, and 15-18 rejected under 35 U.S.C. § 112, first paragraph (Deposit), for the reasons set forth in the objection to the specification, for reasons of record in paper number 6 and paper number 16.

9. Claims 1, 5-13, 15-18 rejected under 35 U.S.C. 112, first paragraph *(written description rejection)*, in light of the amendment of the claims to recite the phrase "one or more" sapA homologs without any upper limit nor defined by a reference strain that comprises the plurality of sapA homolog coding sequences which read on SapCDEF, in addition to other sapA homolog coding sequences not described, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for reasons of record in paper number 13, paragraph 30 and paper number 16, paragraphs 25-26.

10. Claims 1, 6, 8 (amended claim 1) are rejected under 35 U.S.C. 102(b) as being anticipated by Blaser (November 1994) for reasons of record in paper number 6, because the mutant strain exported the mutant S-layer protein in "minimal amounts (see page 456, col. 1, paragraph 2, first half of paragraph).

Response to Arguments

11. The rejection of Claims 1, 5-8, 18 and 10-13, 15-17 under 35 U.S.C. § 112, first paragraph (Deposit), is traversed on the ground that mutant strains have been deposited that enable the claimed mutant strains, or the genes needed in the production of the mutant strains and are therefore enabled over the full scope of the claimed invention.

12. It is the position of the examiner that in light of the perfected Deposit requirement the instant specification has now enabled the sequence contained in the deposited strains/plasmids. Amendment of the claims to recite the Deposited strains and the coding sequences contained therein could obviate this rejection.

13. The rejection of claims 1, 5-13, 15-18 under 35 U.S.C. 112, first paragraph (written description) is traversed by stating that "Applicants submit that is clear to one of ordinary skill in the art that sapB, sapC, sapD, sapE and sapF are not sapA homologs".

14. It is the position of the examiner that a surface associated protein (sap) evidences a conserved sequence for surface association, and a conserved sequence for expression through a Type I secretion system, thus defining the protein as a "sap" homolog. Dworkin et al (1995), teach sapB differs significantly from sapA only in the 5' region encoding the first 183 amino acids (see Dworkin et al, page 15097, col. 2, paragraph 1 and Figure 2 "hatched boxes show sapA and sapB region of coding identity). Evidence is provided in Dworkin et al that sapA and sapB are homologs of one another based upon conserved amino acid identities; additionally sap C,D, E and F are also homologs of sapA.

The acronyms assigned to the "homologs" do not define any specific chemical structure or biological function, but define them to evidence a conserved surface association (see Blaser et al , abstract B014, 1994) and a common mode of expression to the surface, thus defining the molecules to share homology as surface associated molecules.

Additionally, the term "homolog" is generally understood to define an evolutionary relatedness, and not to define any specific sequence or function. The now claimed genus of molecules contained or modified in mutant strains of C.fetus have not been so described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. It is the position of the examiner that while the Deposit has been made to enable a species of the now claimed genus of molecules, the claims are not limited to the Deposited strains and the genes contained therein; the genus has not been enabled over the full scope of the claims.

15. The rejection of claim 10 under 35 U.S.C. 112, first paragraph (written description) is traversed on the grounds that the claimed strain is a RecA mutant strain and a recA mutant of C.fetus strain has been deposited as PTA-4753.

16. It is the position of the examiner that claim 10 does not recite the deposited strain, and is directed to a genus of strains with any type of RecA mutation, and expresses any sapA homolog, the source and sequence of the sapA homolog not being limited to a C.fetus S-layer proteins. Amendment of claim 10 to recite the claim limitations utilized to traverse the rejection could obviate the rejection of the claim; Applicant's arguments are not commensurate in scope with the instantly claimed invention.

17. The rejection of claim 15 under 35 U.S.C. 112, first paragraph (written description) is traversed on the grounds that the claimed E.coli strain modified to express the surface array proteins C,D,E,F of C.fetus has been deposited as PTA-4750 and the plasmid in this strain can readily be used to construct the claimed bacterial strain.

18. It is the position of the examiner that claim 15 does not recite the deposited strain, and is directed to a genus of E.coli strains that comprise one of plurality of coding sequences from C.fetus that encode surface array proteins C,D,E and F but the instant specification has only

enabled a single species of the recited genus. Amendment of claim 15 to recite the claim limitations utilized to traverse the rejection could partially obviate the rejection of the claim, specifically amendment of claim 15 to be directed to the sequences contained in the deposited strain PTA-4750.

Additionally claim 16 depends from claim 15, and is directed to the expression of a chimeric protein that comprises a sapA homolog and the heterologous protein; the coding sequence for the sapA homolog coding sequence is not defined to be that of C.fetus but is any sapA coding sequence from any source. The genus of genes that encodes sapA set forth in claim 16 has not been described. Applicant's arguments are not commensurate in scope with the instantly claimed invention.

New Grounds of Objection/Rejection

Claim Objections

19. Claims 7, 12, 15, 16 and 17 are objected to because of the following informalities:

a. Claim 7 recites the phrase "said DNA cassette does not has a"; this phrase should recite the term --have-- rather than "has".

b. Claim 12 recites the singular tense "strain", but refers back to a mixture of "strains"; the tense of the nouns is not consistent through out the claim.

c.Claims 15 and 16 show a ". (period)" after the term "coli"; this is not the end of the sentence, nor is it an abbreviation. Removal of the period would place the claim in correct form.

d. Claim 17, line 4 shows a ". (period)" after the word "coli", but also recites additional claim limitations following the period; removal of the period would place the claim in the correct format. Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 112

20. Claims 1, 7, 9 and 18 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 has been amended to require the expression of the heterologous protein in "surface expression of a chimeric protein comprising said heterologous protein". Claim 7 depends from claim 1, and defines the mutant strain do comprise a cassette that "comprises a 3' secretion signal of said sapA homolog and sequence encoding said heterologous protein inserted upstream of said secretion signal, but said DNA cassette does not has a 5' LPS binding region of said sapA homolog".

While a species of the mutant strain recited claim 7 could be made, the combination of claim limitations set forth in newly amended claim 1 does not compliment the mutant strain of claim 7 which would secret the mutant protein, but it would not be surface attached as the sequence required for surface attachment which is encoded by the 5' nucleotide sequence is missing in the mutant strain of claim 7 through the recitation of the negative limitations set forth in claim 7 "said DNA cassette does not have a 5' LPS binding region of said sapA homolog".

A strain that would secret the heterologous protein would not evidence a surface associated/attached chimeric protein that would remain on the surface of the mutant C.fetus strain. The claim limitations set forth in claim 7 are not in agreement with the claim limitation set forth for the mutant strain defined in amended claim 1 .

Claim 7 defines a sub-genus of species not disclosed in the instant specification; claim 7 recites New Matter. Amendment of claim 7 to omit the claim limitations that were newly added to claim 1, and set forth in independent form could possibly obviate this rejection.

Claim 9 depends from claim 1, the scope of claim 18 being encompassed by claim 1, and claims 5-8 depending from claim 1, and is directed to a method of immunizing a host (claim 9,

dependent from claims 5 and 1). The mutant strains of claim 1, must surface express a chimeric protein (heterologous protein/SapA homolog protein chimera), but the mutant strains of claim 18 are not required to express the heterologous sequence, and only must have one sapA homolog that is not mutated. The method of claim 9 would not induce an immune response against the heterologous protein immunogen that is not expressed; the combination of claim limitations set forth in claim 18, relative to claim 1, and claim 9, sets forth a sub-genus of species that do not evidence original descriptive support in the instant specification. Claims not evidencing original descriptive support, also are not enabled.

21. Claims 6, 11, 13 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 should recite --further-- prior to the term "comprising on line two. Claim 6 defines a species of invention that has two 5' LPS binding regions and two 3' secretion signal regions; this combination of claim limitations is confusing, in light of the fact that the sapA homolog of claim 1, from which claim 6 depends already has a 5' LPS binding regions and two 3' secretion signal region. Clarification of the claimed invention is requested.

Claim 7 depends from claim 1, and recites the phrase "said DNA cassette comprises a 3' secretion signal of said sapA homolog". In light of the fact that the DNA cassette has been inserted into the sapA homolog that already has a 3' secretion signal, the mutant C.fetus strain of claim 7 has two 3' signal sequences based upon the recited claim language. Will the chimera of the sapA homolog together with the heterologous coding sequence result in a truncated sapA homolog, or no sapA homolog being expressed based upon where in the coding sequence the heterologous sequence is inserted ? The invention of claim 7 is confusing in light of duplicate 3' secretion signal would be contained in the insertion region and the sapA homolog insertion. Clarification of how many signal sequences are associated, and what is actually expressed in the

chimera of claim 7 is requested in light of what follows the first 3' signal sequence, may or may not result in a chimeric protein.

Claim 11 recite a "wherein" clause and depends from claim 10. While a "wherein" clause set forth in a dependent claim can clearly further limit an independent claim, a "wherein" clause does not add additional components, but further characterizes what has been defined in the independent claim. Claim 11 could be made clear by amending the claim to recite the phrase --further comprises--.

Claim 12 recites the phrase "expresses only one S-layer protein comprising a heterologous antigen and a sapA homolog". This phrase is confusing in light of the fact that a heterologous antigen S-layer is one antigen and the recitation of the additional S-layer set forth through the phrase "a sapA homolog" defines two S-layer proteins, and the claim states that only one S-layer protein is expressed. The heterologous antigen is not defined, not to be a heterologous S-layer protein antigen. No heterologous coding sequence has been added to produce the mutant strains. The heterologous antigen is there for a heterologous S-layer antigen relative to the parent wild-type strain. The heterologous antigen and the sapA homolog reads on strains that comprise two S-layer proteins and the claim recites the phrase "only one S-layer protein". The combination of claim limitations is unclear relative one to another. Clarification is requested.

Claim 13 depends from claim 12 and recites the phrase "to the antigens". As claim 12 only recites the singular tense of the term "antigen"; what antigens does the term set forth in claim 13 refer?

Claim 13 recites the phrase "pharmacologically effective dose". The term "pharmacologically" lacks antecedent basis in the claimed method. The term --immunizing--evidences antecedent basis in the preamble of claim 13. An immunizing dose and a pharmacological dose are not necessarily one in the same. The recitation of terms that define different actions is confusing; immunizing and pharmacologically. Amendment of the claim to recite language that is consistent with the recited intended use of the method would make the

claim clear. What is pharmacological about the mutant strain of C.fetus or the amount of the dose?

Claim 18 depends from claim 1 which recites the phrase "a sapA homolog", while claim 18 recites the phase "contains from about 7 to about 9 sapA homologs"; the phrase "about 7 to 9 sapA homologs" lack antecedent basis in claim 1 from which it depends.

Claim 18 defines a mutant strain in which "all but one of said sapA homologs are altered" and depends from claim 1 which only comprises a single altered sapA homolog. How can both conditions be true simultaneously? The combination of claim limitations set forth in newly amended claim 1 is contradicted in claim 18, wherein the mutant strain of claim 1 only has a single sapA homolog mutated through insertion of a heterologous coding sequence and the strain of claim 18 does not require the surface expression or even expression of the sapA homologs into which the heterologous sequence has been inserted and one sapA homolog is left unaltered, thus defining a strain in which a single sapA is expressed normally that does not produce a chimeric protein as required by claim 1. The combination of the claim limitations of claim 1 and claim 18 taken together are unclear.

Claim 18 is not further limiting of claim 1 which requires the surface expression of a chimeric protein of a SapA/heterologous protein to be present on the surface of the mutant, which claim 18 which depends from claim 1 does not require the expression and association of a chimeric protein of a SapA/heterologous protein to be present on the surface of the mutant strain, thus broadening the scope of claim 18 relative to claim 1. While the strain of claim 18, may evidence more mutations, the surface expression of a chimeric protein is not, which is the critical distinguishing characteristic of the strain of claim 1.

Claim Rejections - 35 U.S.C. § 102

22. Claims 1, 5, 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Dworkin et al (1995, J. Biological Chemistry, Vol. 270).

Dworkin et al disclose the claimed invention directed to a genetically mutated strain of C.fetus (strain 82-40 LP3, see page 15094, Table 1), wherein the strain comprises a DNA cassette (first and second sapA homologs expressed) into the coding sequence of a sapA homolog of said strain and encodes a heterologous protein (two proteins in S-layer, 97 kDa and 127 kDa (heterologous to wild type strain that only expressed the 97 kDa protein), the expression of which results in a chimeric protein comprising the heterologous protein (surface associated proteins in the S-layer (see Table 1 legend, page 15094) . The heterologous protein is from an animal pathogen (Campylobacter fetus) Inherently the disclosure of Dworkin et al anticipates the instantly claimed invention.

Conclusion

23. This is a non-final action.

24. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

25. Boot et al (September 1996) is cited to show expression, secretion and antigenic variation of bacterial s-layer proteins from C.fetus.

26. Blaser et al (1990) is cited to show the coding sequence for C.fetus surface array protein and cloning vectors that comprise the coding sequence for the Sap protein.

27. Blaser (Nov. 1993, Am.J.Med.Sci) is cited to show a teaching with respect to an 18-residue stretch near the carboxy terminal (amino acids 672-689) that has the characteristics of a membrane spanning structure suggesting that it may play a role in export (C.fetus sequence for strain 23D).

28.Dworkin et al (J.of Bacteriology, Apr. 1995) is cited to show an LPS binding domain in C.fetus S-layer protein (see title).

29. Dworkin et al (Dec. 1997) is cited to show the role the recA encoded protein plays in C.fetus S-layer variation due to recombination events.

30. Dworkin et al (abstract D-193) is cited to show that the 3' end of the open reading frame of C.fetus sapA2 has increasing diversity, and a conserved sequence at the 5' (encoded N-terminal) end; and suggests that S-layer protein expression results from rearrangement of complete gene copies from a single large locus containing multiple sapA homologs.

31. Guerry, P et al (Feb. 1994, best copy available) is cited to show recA mutants of C.jejuni and their utilization in method of vaccination and as attenuated vaccines; the reference suggests the construction of recA mutant strains in other Campylobacter species (see Discussion section, paragraph 2, middle to end of paragraph).

32. Salama et al (1995) is cited to show a sapA homolog of C.fetus (see abstract, Table 3, Figures 1 and 2)

33.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first Friday of each two week period.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for this group is (703) 308-4242.

The Group and/or Art Unit location of your application in the PTO will be Group Art Unit 1645. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to this Art Unit.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196. Vgp
March 26, 2003

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